Remarks

Claims 1-19 are pending. Claims 20-29 have been cancelled as drawn to a non-elected invention.

Claim 1 has been amended to provide a step in which the concentration of factor indicative of osteoporosis is measured relative to a normal control. Claims 1, 12, 13 and 15 have been amended to correct antecedent basis. Claim 3 has been amended to clarify the claim language.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-19 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled for detection of osteoporosis caused by an infectious agent other than a bacteria. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 1 is directed to a method of detecting osteoporosis by (1) obtaining a sample of bone-related tissue, and (2) measuring a marker selected from the group consisting of infectious agents, factors produced by infectious agents, and heat shock proteins (HSPs) produced in response to an infectious agent. Claims 12 and 13 further define the marker as being selected from the group consisting of bacteria, viruses, protozoa, parasites, fungi, bacterial produced factors, viral produced factors, protozoal produced factors, parasitic produced factors and fungal produced factors. The specification demonstrates actual examples of methods of detecting osteoporosis by measuring bacteria, bacterial produced factors, and HSPs (also known as chaperones).

The test for enablement is whether one skilled in the art would be able to practice the claimed method without undue experimentation, not whether or not the examiner believes the results would have commercial or clinical relevance.

Accordingly, one must first look at the claim language to see what is being claimed:

A method of detecting osteoporosis in a individual to be tested comprising:

a) obtaining a sample of a bone related tissue or cells; and

b) assaying the concentration of at least one marker selected from the group consisting of infectious agents, a factor produced by an infectious agent, and heat shock proteins (HSPs) produced in response to an infectious agent, and

c) comparing the concentration of the at least one marker with the concentration of the marker in a sample of the same bone related tissue or cells from a control individual who does not have osteoporosis.

Methods of obtaining a sample of bone related tissue or cells is certainly not difficult – doctors routinely biopsy tissues from patients. This would need to be done from the patient who is to be tested for osteoporosis, as well as from normal controls.

Assays for infectious agents, factors produced by infectious agents (such as those listed in the dependent claims, including bacterial, yeast, parastic and viral protein and nucleic acid), and heat shock proteins (well known in the art) are also routine.

It is similarly routine to compare the levels of these proteins or nucleic acids or infectious agents from the individual to be tested with those from the normal controls.

Accordingly, undue experimentation is not needed for one skilled in the art to carry out the the claimed method. MPEP § 2164.01, reciting *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), emphasizes that the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims require the measurement of various markers, and the comparison of these measurements to standards or subsequent measurements in the same individual. While measurement of the various factors may require some experimentation, those skilled in the art typically engage in such experimentation. Quantification of bacteria, viruses, fungi, protozoa, parasites and their respective factors is an experimentation typical of the art. Therefore, claims 1-19 are enabled by the specification.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 2-5 and 7-11 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it applies to the claims as amended. The examiner's careful review in this regard is appreciated.

Claim 2 recites comparing a marker concentration of a first assay with concentrations of a second or more assays from the same individual over a period of time or against a standard concentration. It is believed the objection here is with respect to the word "assay" and this has been replaced with the term "marker", which also corrects the antecedent basis. "A period of time" is defined in the specification as ranging from several hours to several years. See page 27, lines 4-8. Moreover, measurements taken over varying lengths of time are not uncommon in diagnostic tests. One skilled in the art would be able to understand the scope of the claims and

what constitutes infringement of the patent. The limitation about comparison with a known, or control, sample has been moved into claim 1.

Claim 3, as amended, recites obtaining a sample under conditions which do not induce *a change in the amount of HSPs* in the subject, wherein the marker is an HSP. The claim has been amended to clarify that the sampling itself should not induce an HSP response, not that there is no HSP response at the time of sampling. Insertion of the definition of the marker as an HSP should correct antecedent basis for claims 4, 5, and 7-11.

Rejection Under 35 U.S.C. § 103

Claims 1-6, 8 and 11 were rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/13204 to Findlay in view of Nair, et al., Calcif. Tissue Int. 64(3): 214-218 (1999). Claims 1, 12-14 and 19 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Findlay in view of Reddi, et al., J. Bone Min. Res. 13(8): 1260-1266 (1998). Applicants respectfully traverse these rejections to the extent that they are applied to the claims as amended.

Findlay

Findlay describes a method of predicting or diagnosing a skeletal disorder in an individual including the steps of obtaining a body tissue or fluid sample, measuring the level of at least **one regulator or marker of bone remodeling**, and comparing the level to a standard (see abstract). Findlay describes the regulators as being internal regulators of bone growth, such as growth factors and cytokines and associated proteins (see page 4, lines 16-32).

Nair

Nair describes the examination of a number of bacterial and mammalian molecular chaperones for activity in the murine calvarial bone resorption assay. Nair discloses that both bacterial and mammalian chaperones are potent inducers of bone resorption and appear to have the capacity to modulate the cellular processes in bone explant cultures, resulting in resorption of the calcified matrix.

Reddi

Reddi discloses that bacterial cpn60 from *E. coli* stimulates bone resorptive activity and formation of osteoclasts in culture. Reddi suggests that bacterial chaperonins may play a role in osteolysis associated with bone disease and perhaps have a role in other bone loss disorders such as osteoporosis. In addition, Reddi discloses the presence of a potent bone-resorbing protein on the surface of *Actinobacillus actinomycetemcomitans*, which causes periodontal disease.

Applicant's claims are not drawn to measurement of bacterial HSPs, however, but to HSPs which are induced by infection. These would be mammalian HSPs, endogeous to the cells and tissues, whose endogenous levels are increased by infection.

Summary

Findlay teaches measurement of *internal regulators* of bone resorption, while the claims in this application are drawn to measurement of *causative factors* of bone resorption (ie, bacteria, parasites, etc.) or HSPs, which are induced by infection. None of the art teaches measurement of an infectious agent, a component thereof or an HSP which is induced by an infectious agent, to predict that an individual has osteoporosis.

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AMENDMENT AND RESPONSE TO OFFICE ACTION

Allowance of claims 1-19, as amended, is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, November 26, 2003, to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Patrea Pabst

Date: November 26, 2003

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